REMARKS

Claims 1, 12, 13, 21, 24, 25, 29, 31, and 39-60 are pending and are under examination. Claims 12, 29, 39, 40, 44, 52, 54, and 56-58 have been cancelled herein without prejudice or disclaimer.

Claims 1, 13, 21, 24, 25, 31, 41-43, 45-51, 53, 55, 59, and 60 have been amended herein. Support for these amendments may be found in the application as originally filed. In particular, support for the amendments to Claims 1 and 43 may be found, for example, in the original claims and also at least on page 4, paragraph [0048]; page 7, paragraph [0085]; page 18, paragraph [0182]; pages 16-18, Examples 1-3; pages 19-26, Tables 1-3; and page 27, Table 5 of the published application. Support for the amendments to Claims 13, 21, 24, 25, 31, and 41 may be found in original Claim 1. Support for the amendments to Claims 42 and 60 may be found in the original claims. Support for the amendments to Claims 45-51, 53, 55, and 59 may be found in original Claim 43. Accordingly, no new matter is added by the amendments to the claims.

The Rejection of the Claims Under 35 U.S.C. 112, First Paragraph Is Rendered Moot

Claims 1, 12, 13, 21, 24, 25, 29, 31, and 39-60 were rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the written description requirement. Applicants respectfully submit that the present amendments to the claims render this rejection moot.

The Office Action stated that the claims are drawn to methods comprising investigating a genus of mutations at positions 11, 47, 50, 76, 83, 91, or 95; and positions 32, 33, 43, 46, 48, 54, 58, 71, 79, 82, or 84 of the protease protein sequence of an HIV-1 strain. However, the Office Action asserted that the application discloses only one to three species for each of the amino acid positions. The Examiner cited Colonno *et al.* (2004, J. Infect. Dis. 189:1802-10) as teaching that the substitutions of two different amino acids at the same amino acid position do not necessarily result in similar resistance properties.

Applicants have amended Claim 1 to delete reference to positions 47 and 50, and to specify that the mutation at position 11 is isoleucine (I) or leucine (L) instead of valine (V); the mutation at amino acid position 34 is glutamine (Q) instead of glutamic acid (E);

the mutation at position 76 is valine (V) instead of leucine (L); the mutation at position 83 is aspartic acid (D) instead of asparagine (N); the mutation at position 91 is alanine (A), valine (V), or serine (S) instead of threonine (T); and the mutation at position 95 is phenylalanine (F) instead of cysteine (C).

Applicants have amended Claim 43 to delete the reference to position 79, and to specify that the mutation at position 32 is isoleucine (I) instead of valine (V); the mutation at position 33 is phenylalanine (F) instead of leucine (L); the mutation at position 43 is threonine (T) instead of lysine (K); the mutation at position 46 is isoleucine (I), leucine (L), or valine (V) instead of methionine (M); the mutation at position 48 is methionine (M), serine (S), or valine (V) instead of glycine (G); the mutation at position 54 is alanine (A), serine (S), threonine (T), leucine (L), valine (V), or methionine (M) instead of isoleucine (I); the mutation at position 58 is glutamic acid (E) instead of glutamine (Q); the mutation at position 71 is leucine (L), isoleucine (I), valine (V), or threonine (T) instead of alanine (A); the mutation at position 82 is alanine (A), phenylalanine (F), serine (S), or threonine (T) instead of valine (V); and the mutation at position 84 is alanine (A) or cysteine (C) instead of isoleucine (I). Support for the correlation of these particular mutations and reduced susceptibility to amprenavir is described in the specification, *e.g.*, generally at page 7, paragraph [0085]; pages 17-18, paragraphs [0181]-[0182], and more particularly at pages 16-18, Examples 1-3; pages 19-26, Tables 1-3; and page 27, Table 5 of the published application.

Applicants respectfully submit that the specification describes the subject matter of the claims as amended herein such that one skilled in the art would understand that Applicants were in possession of the claimed invention at the time the application was filed. Therefore, Applicants respectfully request the rejections under 35 U.S.C. § 112, first paragraph be withdrawn.

The Rejection of the Claims Under 35 U.S.C. 103(a) Is Traversed or Rendered Moot

Claims 1, 12, 13, 21, 24, 25, 29, 31, and 39-60 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Carrillo *et al.* (1998, *J. Virol.* 72(9):7532-41)

(hereinafter "Carrillo") in view of Gilden (1999). Applicants respectfully submit that the pending claims as amended are not obvious over the teachings of Carrillo and Gilden.

The Office Action asserted that Carrillo teaches the detection of mutations in the HIV-1 protease gene after treatment with a protease inhibitor. The Office Action noted that the mutations identified in Carrillo are L33I, E34A, E34K, A71V, L76V, V82A, and T91S when compared to the sequence of a wild type NL4-3 strain protease. The Office Action noted that Carrillo teaches that the disclosed mutations confer reduced susceptibility to **ABT-378**, rather than **amprenavir**. The Office Action asserted that Gilden teaches that amprenavir resistance mutations at codons 10, 46, and 54 contribute to broad cross-resistance and that ABT-378's activity is hobbled by many of the same protease mutations that affect amprenavir resistance. Therefore, the Office Action asserted that it would have been obvious to one skilled in the art to modify the method of Carrillo to determine reduced susceptibility to amprenavir with a reasonable expectation of success based on the teaching of Gilden.

As discussed above, Applicants have amended Claim 1 to identify specific mutations at each of the positions listed (*i.e.*, the mutation at position 11 is isoleucine or leucine, the mutation at amino acid position 34 is glutamine, the mutation at position 76 is valine, the mutation at position 83 is aspartic acid, the mutation at position 91 is alanine, valine, or serine, and the mutation at position 95 is phenylalanine). Applicants have amended Claim 43 to identify specific mutations at each of the positions listed (*i.e.*, the mutation at position 32 is isoleucine; the mutation at position 33 is phenylalanine; the mutation at position 43 is threonine; the mutation at position 46 is isoleucine, leucine, or valine; the mutation at position 48 is methionine, serine, or valine; the mutation at position 54 is alanine, serine, threonine, leucine, valine, or methionine; the mutation at position 58 is glutamate; the mutation at position 71 is leucine, valine, or threonine; the mutation at position 82 is alanine, phenylalanine, serine, or threonine, and the mutation at position 84 is alanine or cysteine).

Carrillo and Gilden do not teach or remotely suggest the majority of these specific mutations listed in Claim 1 (with one exception – L76V), or the combination of one of the mutations in Claim 1 with one of the mutations listed in Claim 43. Rather, Carrillo teaches

that certain mutations (*i.e.*, L33I, E34A, E34K, A71V, L76V, V82A, and T91S) confer resistance to **ABT-378**. *See, e.g.*, Abstract. Gilden merely mentions positions 10, 46, and 84 as being mutations that affect both ABT-378 and amprenavir resistance, without identifying particular mutations. *See, e.g.*, Gilden, second paragraph under "ABT-378."

As discussed previously, one of skill in the art would not expect that the presence of a particular mutation in the protease gene that confers increased susceptibility to one protease inhibitor (*e.g.*, ABT-378) would necessarily confer susceptibility to a different protease inhibitor (*e.g.*, amprenavir). As the Examiner acknowledged, Colonno *et al.* teach that substitutions of two different amino acids at the same amino acid position in the protease gene do not necessarily result in similar resistance properties. Similarly, Colonno *et al.* teach that a particular mutation at position 50 of the protease gene (I50V) **reduces susceptibility** to one protease inhibitor (*i.e.*, atazanavir), and **increases susceptibility** to another protease inhibitor (*i.e.*, amprenavir). *See* page 1808, Table 4. In addition, although Gilden mentions that three of the protease mutations identified that affect amprenavir resistance also affect ABT-378, the sponsor of ABT-378 (Abbott Laboratories) had claimed that there is little cross-resistance between ABT-378 and other protease inhibitors. *See* Gilden, second paragraph under "ABT-378." Moreover, Carrillo and Gilden do not identify any shared structure or motif correlating with the function (decreased drug susceptibility) that would suggest that any particular mutation would be likely to confer decreased susceptibility to both ABT-378 and amprenavir. Therefore, one skilled in the art would not have a reasonable expectation of success that any particular mutation of the many possible mutations that affect ABT-378 susceptibility would necessarily also affect amprenavir susceptibility.

For at least these reasons, Carrillo and Gilden do not teach, suggest, or provide a reasonable expectation of success to arrive at the presently claimed invention. Therefore, Applicants respectfully request the rejections under 35 U.S.C. § 103(a) be withdrawn.

CONCLUSION

Applicants submit that the foregoing is a full and complete response to the Non-Final Office Action mailed September 8, 2010. In view of the foregoing amendments and remarks, each of the claims remaining in the application is in condition for immediate allowance. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the outstanding rejections.

Applicants have submitted herewith a petition for a one month extension of time, along with the appropriate fee therefore. No additional fees are believed due; however the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account number 11-0855.

If the Examiner believes that any informalities remain in the case that may be corrected by Examiner's Amendment, the Examiner is invited to telephone the undersigned attorney at (404) 541-6662 or Dr. Cynthia B. Rothschild at (336) 747-7541 to discuss any questions relating to the application.

Respectfully submitted,

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